UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/593,259 | 07/26/2007 | Remo Kranich | 1043.0005-00000 | 6454 |

68540 7590 12/11/2009

O'BRIEN JONES, PLLC
8200 Greensboro Drive
Suite 1020A
McLean, VA 22102

| EXAMINER | |
|---|---|
| CORNET, JEAN P | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1628 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 12/11/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@OBRIENJONES.COM
susanne.jones@obrienjones.com
michelle.obrien@obrienjones.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/593,259 | KRANICH ET AL. | |
| | Examiner | Art Unit | |
| | JEAN CORNET | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-16* is/are pending in the application.

4a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. The amendment filed on 9/15/2009 in response to the Non-Final office Action of 6/15/2009 is acknowledged and has been entered. As stated in the previous Office Action, claims 14-16 were interpreted as being directed to products as well as regarding product embodiment(s) therein. Since Applicant amended the claims that are now related to method claims, all the rejection related to these claims will be withdrawn as they are now related to nonelected invention.

Newly submitted claims 14-16 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: these claims were initially interpreted as having product embodiment(s) and now Applicant amended them to method claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 14-16 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 11-16 are pending. 14-16 are withdrawn and 11-13 are currently under consideration.

**Rejections withdrawn:**

**Rejections under 35 U.S.C. § 112, ¶2 and § 101**

2. Applicant's arguments see page 6 with respect to § 112, ¶2 and § 101 have been fully considered and are persuasive due to claims amendment. The rejection of claims 14-16 has been withdrawn.

**Claim Objections**

3. Applicant's argument with respect to objection of claims 14-16 has been fully considered and rendered moot due amendment.

**Rejections under 35 U.S.C. § 112, ¶2**

4. Applicant's arguments with respect to § 112, ¶2, as being indefinite have been fully considered and are persuasive due to claims amendment. The rejection of claims 11-16 has been withdrawn.

**Rejections under 35 U.S.C. § 112, ¶1**

5. Applicant's arguments with respect to § 112, ¶1, as being not enabling for the prophylaxis of inflammatory disorders have been fully considered and are persuasive due to claims amendment. The rejection of claims 15 has been withdrawn.

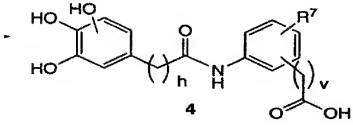
**Rejections Maintained:**

***Claim Rejections - 35 USC § 103***

6. **Claims 11, 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Blaakmeer et al. (Structure-Activity relationship of isolated avenanthramide alkaloids and synthesized related compounds as oviposition deterrents for Pieris Brassicae, Journal Of Natural Products, Vol. 57, No. 8, pp. 1145-1151, August 1994) cited in 892 form in view of Appledoorn et al (Rational Optimization of a short Human P-selectin-binding Peptide leads to nanomolar affinity antagonists, The Journal of Biological Chemistry Vol. 278, No. 12, issue of March 21, pp.**

**10201-10207, 2003) cited in the IDS and Patani et al. (Bioisosterism: A Rational Approach in Drug Design, Chemical Rev., 1996, 96 (8), 3147-3176) cited in the 892 form**

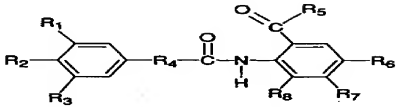
The instant application is drawn to a pharmaceutical composition comprising at least one of the formula C or D and a pharmaceutically acceptable carrier which is useful in a medicine.




4

With v is 2, R7 is H and both substituents can be anywhere on the ring.

Blaakmeer teaches structure-activity relationship investigation of several compound isolated from the eggs of Pieris brassicae, large cabbage butterfly and eight synthesized related compounds as ovposition deterrents for the insect where their activities were tested. The specie compound 10, 2-[(3, 4, 5-trihydroxy-benzoyl) amino}-3, 5-dihydroxybenzoic acid of the general formula below (Abstract and page 1146).



Where R1, R2 and R3 are OH; R4 is $CH_2$=$CH_2$; R5 is OH; R6 is OH; R7 is H and R8 is OH then the species of this compound is compound 10(page1146), then Blaakmeer's compound reads on the instant claim compound of formula C, when the carboxyl group with the (CH2) v is on the carbon positioned to the left of the amino group and R7 is anywhere of the instant compound.

Blaakmeer does not teach a pharmaceutical composition using the compounds of his invention and a pharmaceutically acceptable carrier.

Appledoorn teaches pentapeptide core motif as potent antagonists for P-selectin using two-step combinatorial chemistry approach. These pentapeptides compounds with Gallic acid-substituents proved to be potent inhibitors of P-selectin binding. A dedicated library of peptides derivatives was generated by introducing seven substituents at the N and C termini of the motif. The length and rigidity of the connective spacer can be varied (abstract). These compounds with the number of exposed hydroxyl groups on the first ring appear to be critical for its affinity, because mononbenzoic acid derivatized and dihydrobenzoic acid derivatized were much less effective than the trihydroxylated counterparts (page 12205 left column last paragraph). P-selectin antagonists were screened for intervention of inflammatory disease (page 10202, results)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the compounds taught in Blaakmeer using combinatorial chemistry as suggested by Appledoorn as P-selectin ligands since Patani suggests monovalent substitution by hydroxyl group in place of hydrogen has recently been used in drug design (page 3152, table 9).

It would have been obvious as well to formulate a pharmaceutical composition to include a pharmaceutical acceptable carrier system such as solvents, and other conventionally known adjuvants since it is well know in the art when making a pharmaceutical composition to include a carrier for drug delivery and since Appledoorn teaches that these ligands offer great therapeutic potential and would greatly benefit from further optimization studies. The technique and skill for adding and selecting a carious materials are well within the level of the ordinary skilled artisan and commonly practiced in the state of the art and thus, obvious absent evidence to the contrary.

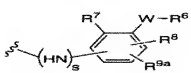
One would have been motivated to combine the references and modify the compounds via combinatorial chemistry with reasonable expectation of success, because they share the same core structures that is three hydroxyls groups on the ring with a peptide bonds, and pertinent to the problem which applicant concerns about. MPEP 2141.01 (a).

**Applicant's arguments**

7. In response to this rejection, Applicant asserts the following:

A. No prima facie case of obviousness had been established because the claims as a whole would not have been obvious in view of Blaakmeer, Appledoorm and Patini when considered as whole. Specifically Blaakmeer disclosed compound that do not read on the claimed compounds and one of ordinary skill in the art would not have been motivated to modify the compound disclosed in Blaakmeer.

B. The examiner must focus the obviousness rejection on the claimed compounds instead of compound (4) that is disclosed in the specification. As is readily apparent upon consideration of variable Y', the amine part of the structure Of the claimed compound is quite different where if the claimed compound is chosen to have following Y' substituent



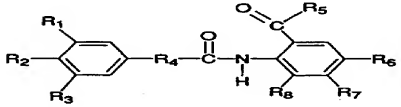

The carboxylic group (i.e. W is -(CH2)v, V is O, and $R^6$ is $CO_2H$), if chosen, may not be in the ortho-position, $R^7$ may be H, and $R^8$ and $R^{9a}$ may not be OH. For this reason the compounds of Blaameer, including compound 10, fail to teach or suggest the claimed compound.

These arguments have been carefully considered, but are not found persuasive.

**Response to Applicant's arguments**

8. In response to Applicant's argument of part (A), In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Examiner recognizes that it is the combination of all of the cited and relied upon references, which make up the state of the art with regard to the claimed invention. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the present case, compound 10; 2-[(3,4,5-trihydroxy-benzoyl)amino}-3,5-dihydroxybenzoic acid of the general formula:



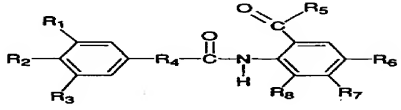

taught by Blaakmeer clearly reads on the claimed compound (4), where R1, R2 and R3 are OH; R4 is $CH_2$=$CH_2$; R5 is OH; R6 is OH; R7 is H and R8 is OH. Appledoorn clearly teaches that pentapeptides core motif as potent antagonist for P-selectin having similar core structure as compound 10 for the intervention of inflammatory disease can be modified using combinatorial chemistry. At last, Patini suggests monovalent substitutiion by hydroxyl group in place of hydrogen has recently been used in drug design. Thus

one would have been motivated to modify the compound 10 taught by Blaakmeer and replace the OH with Hydrogen to arrive at the claimed invention.

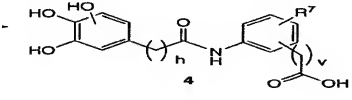
In response to the part (B) argument, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969).

Examiner interprets the amine, R8 and R9a part of the Y' structure of the claimed invention can be any where on the ring except where R7 and W is bonded. Therefore if the amine is bonded to the ortho-postion (to the right of the W-R6), compound 4 of the specification reads on claim 11. Since the elected specie was free of the art, examination was expanded to the next specie which was compound 4. The assertion that "the carboxylic group (i.e. W is - (CH2) v, V is O, and $R^6$ is $CO_2H$), if chosen, may

not be in the ortho-position, $R^7$ may be H, and $R^8$ and $R^{9a}$ may not be OH" is not in the claim. Thus compound 10

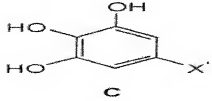


of Blaakmeer, where R1, R2 and R3 are OH; R4 is $CH_2$=$CH_2$; R5 is OH; R6 is OH; R7 is H and R8 is OH in view of Patini that suggests monovalent substitutiion by hydroxyl group in place of hydrogen clearly reads on the instant compound 4, where h =1, 2 or 3 with v is 0, R7 is H



4

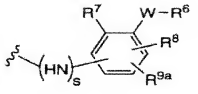
Instantly claimed compound 4 reads on claim 11



C

Where X is

And Y' is




Thus it would have been obvious to one of ordinary skill in the art to combine the reference and substitute Blaakmeer's compound as suggested by Appledoorn via combinatorial chemistry to replace the OH with H as suggested by Patini to formulate a pharmaceutical composition that includes a pharmaceutical acceptable carrier system such as solvents, and other conventionally known adjuvants since it is well known in the art to include a carrier when making a pharmaceutical composition and since Appledoorn teaches these ligands offer great therapeutic potential and would greatly benefit form further optimization studies.

***Conclusion***

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free)? If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642